REMARKS

In the Office Action dated January 27, 2005, claims 39-47, 52, and 53, all of the claims under consideration of the subject patent application, were rejected. By amendment above, claims 39, 52, and 53 have been rewritten. New claims 54-73 have been added. Support for the amendments in claims 39, 52 and 53 can be found on page 12 lines 23-27 of the specification. Support for new claims 54-73 can be found in previously presented claims 39-47, 52 and 53 and on page 12 lines 23-27 of the specification.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 39-47, 52 and 53 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Armitage et al. (WO 9220334) in view of Gregory et al. (5,262,179). According to the Examiner, Armitage et al. et al disclose "a pharmaceutical composition comprising ibuprofen salt in racemic mixture of S-ibuprofen, such as alkaline earth metal salts, for example the sodium salt of ibuprofen, and a carrier, a compressible filler component such as lactose, microcrystalline, and calcium phosphate, combined with a disintegrating component such as maize starch and lubricating agents." The Examiner asserts that Armitage et al. et al also discloses the effective amounts of the ingredients. However, according to the Examiner Armitage et al. does not expressly disclose the employment of the particular sodium carbonate or sodium bicarbonate in an amount of 3-20% by weight in the ibuprofen dosage, and the particular amount of sodium salt of ibuprofen. According to the Examiner, Gregory et al discloses masking the unpleasant taste of ibuprofen salts by incorporating an alkali metal bicarbonate into the dosage form. Specifically, the Examiner asserts that Gregory et al disclose the particular amounts of the

ingredients as claimed in the present invention. According to the Examiner it would have been obvious to employ the particular sodium carbonate or sodium bicarbonate in an amount of 3-20% by weight in the ibuprofen dosage of Armitage et al. and to optimize the amount of sodium salt of ibuprofen. According to the Examiner, the motivation to combine Gregory et al with Armitage et al. et al is that it was known that ibuprofen salts have an unpleasant taste and it is advantageous to provide a dosage form which will mask this unpleasant taste by incorporating the sodium carbonate or sodium bicarbonate according to Gregory et al. Therefore, the Examiner asserts the claimed invention is obvious over the teachings of the prior art.

Furthermore, applicant's arguments in response to the previous Office Action were considered not persuasive by the Examiner. Applicant argued that Armitage et al. aims to solve a completely different problem than Gregory et al. and also than the problem addressed by the invention of the present application. According to the Examiner the teaching of Gregory et al provides the motivation for using sodium salts for masking the taste of sodium ibuprofen. In addition, applicant argued that the dosage form is swallowed as a whole and therefore masking the taste of the active ingredient would not be a consideration. In contrast, the Examiner asserts that taste masking is a consideration because the human mouth is an aqueous environment and some degree of dissolution of the dosage form would occur, exposing the active ingredient. Therefore, there is, according to the Examiner, a motivation to combine the cited prior art references.

In response to the Examiner, applicant submits that claims 39-47, 52, and 53, as amended, are not obvious over Armitage et al in view of Gregory et al. Claims 39-47, 52, and 53 now require the dosage form or formulation to be coated. Such coated dosage forms or

formulations are swallowed as a whole, as defined in the claims. Thus, there is no disintegration or dissolution of the coated dosage form in the oral environment when swallowed as a whole and therefore no dispersion of the active ingredient in the aqueous environment of the human mouth. This is in contrast to the Examiner's assertions. Therefore, no taste masking is required or contemplated for such a coated dosage form or formulation as in claims 39-47, 52, and 53, as amended. For this reason there is no motivation to combine the teaching in Armitage et al with Gregory et al, where Gregory et al teach including sodium bicarbonate as a taste masking component in a dosage form comprising sodium ibuprofen as the active ingredient. Therefore, applicant submits that claims 39-47, 52, and 53 are not obvious over Armitage et al in view of Gregory et al.

Furthermore, applicant submits that the invention of the present application provides an improved compressed dosage form which is swallowed whole and permits delivery of high therapeutic levels of the sodium salt of racemic ibuprofen to the gastrointestinal tract of a patient.

As stated in the present application at page 7, the sodium salt of racemic ibuprofen is a flaky, soft and sticky material. Consequently, it does not lend itself to formulation into a directly compressed dosage form as it typically sticks to the tabletting punches. Moreover, it is also difficult to pre-granulate the sodium salt prior to compression with other excipients. In order to form satisfactory compressed dosage forms of the sodium salt of racemic ibuprofen it is necessary to pre-treat the salt, i.e. milling, etc.

Unexpectedly, the inclusion of sodium bicarbonate or sodium carbonate in the carrier material permits the formation of a satisfactory compressed dosage form of the sodium salt of racemic ibuprofen without the need to initially pre-treat the ibuprofen. Conveniently, it is

therefore possible to use sodium ibuprofen taken directly from a bulk production process, thereby significantly reducing the overall production costs (see page 7, lines 28 to 31 and page 2, lines 12 to 14).

In addition, the inclusion of sodium bicarbonate or carbonate also enhances the compressibility of the pharmaceutical composition comprising the compressible filler and disintegrant. Particularly, the composition used to form the compressed dosage form may be compressed by applying compression forces of standard tabletting machines to produce a compressed dosage form which exhibits improved hardness (i.e. so that it does not break up during further manufacturing steps) while maintaining an acceptable relatively fast disintegration time to permit an onset hastened action (see page 2, lines 1 to 20, page 3, lines 8 to 14). This effect is clearly demonstrated by the results of Tables 1 and 2 and commentary thereon at page 31. The inclusion of sodium bicarbonate or carbonate permits a reduction in the overall amount of compressible filler thereby allowing production of an acceptably sized tablet including a large therapeutic dose of the sodium salt of racemic ibuprofen (page 2, lines 4 to 8 and page 3, lines 7 to 10).

To more clearly define the above mentioned subject matter in which sodium carbonate is included in a dosage form applicant has added new claims 57-73. In addition, applicant submits that Gregory et al teaches away from using sodium carbonate in an oral dosage form because it would increase pH to unacceptable levels (see Gregory et al, column 3, lines 39-42).

Applicant respectfully submits that the invention of claims 39-47, 52, and 53, as amended and new claims 54-73 therefore is not obvious over Armitage et al. (WO 9220334) in

combination with Gregory et al. (5,262,179). Withdrawal of the rejection is respectfully requested.

Claims 39-47, 52 and 53 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Geyer et al. (US 5,380,535) in view of Gregory et al. (US 5,262,179). According to the Examiner, Geyer et al discloses chewable compositions for oral delivery of unpalatable drugs. Further, the Examiner asserts that Geyer et al discloses the compressable fillers of claims 8 and 31 and the disintegrating components of claims 9 and 30. Moreover, according to the Examiner Geyer et al discloses a powder that can be compressed into a tablet comprising ibuprofen, a compressible filler, a disintegrant, sodium bicarbonate, lubricants and flow aids. However the reference does not disclose the crushing strength, disintegration time or compression force as instantly claimed, a salt of ibuprofen or a solid formulation having a layer as instantly claimed. Further, Geyer et al. does not expressly disclose the employment of the particular sodium carbonate or sodium bicarbonate in 3-20% by weight in the ibuprofen dosage, and that the particular sodium salt of ibuprofen may be 40-60%. According to the Examiner Gregory et al discloses masking the unpleasant taste of ibuprofen salts by incorporating an alkali metal bicarbonate into the dosage form. The Examiner asserts that it would have been obvious to employ the particular sodium carbonate or sodium bicarbonate and 3-20% ibuprofen and to optimize the amounts of sodium carbonate or sodium bicarbonate. Further, the Examiner asserts that one of ordinary skill in the art would select optimal parameters to obtain beneficial effects.

Applicant submits that claims 39-47, 52 and 53, as amended are distinct and nonobvious over Geyer et al in view of Gregory et al. In particular, the dosage forms as now claimed are coated and thus do not dissolve or disperse in the aqueous environment of the human mouth

when swallowed as a whole. Therefore, as discussed above, no portion of the active ingredient within a coated solid dosage form is exposed to the oral mucosa if the dosage form is swallowed whole, as the active ingredient is enclosed within the dosage form and therefore not exposed to the oral mucosa and the active ingredient is released in the gastro-intestinal tract as opposed to the oral cavity. Thus, it is typically not necessary to consider taste masking active agents for compressed dosage forms which are swallowed whole.

In light of the above, Applicant respectfully submits that a skilled person would not even consider Geyer et al. or Gregory et al., let alone combine the teaching of these references, in an attempt to provide a compressed solid dosage form adapted to be swallowed whole, as the taste masking issues discussed in Geyer et al. and Gregory et al. are not applicable to coated dosage forms that are swallowed. In addition, as discussed above, applicant added new claims 57-73 to more clearly define the subject matter of the embodiment of the invention which includes sodium carbonate in the dosage form, which inclusion is taught away from in Gregory et al.

Therefore, applicant submits that the use of sodium bicarbonate or sodium carbonate in a compressed coated dosage form or sodium carbonate in a compressed dosage form of the sodium salt of racemic ibuprofen is not obvious over the combination of Geyer et al. and Gregory et al. Applicant respectfully submits that the claimed invention of claims 39-47, 52, and 53-56, and new claims 57-73 therefore is not obvious over Geyer et al. (US 5,380,535) in combination with Gregory et al. (US 5,262,179). Withdrawal of the rejection is respectfully requested.

Applicant submits that the present application is now in condition for allowance.

Reconsideration and favorable action are earnestly requested.

RESPECTFULLY SUBMITTED,					
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